Remarks

Reconsideration of this Application is respectfully requested. The above amendments are believed to present the rejected claims in better form for consideration on appeal. Claims 1, 3, 5-10, 12-14, 16-18, 20-27, 29, 31-37, and 39-44 are pending in the application, with claims 1, 20, and 21 being the independent claims. Claims 1, 5, 6, 12, 13, 20-27, 31 and 40 are sought to be amended. Support for the amendments can be found throughout the specification and original or previously presented claims. Support for the amendments to the independent claims requiring that at least one matrix comprises one or more lysis/disruption/permeabliization compositions or compounds can be found, for example, in Applicants' specification at page 9, lines 7-14, and original or previously presented claims 11, 20 and 30. New claims 41-44 are sought to be added. Support for these new claims can be found in the specification, for example, at page 7, paragraphs 14-15. Claims 2, 4, 11, 15, 28, 30 and 38 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Rejections under 35 U.S.C. § 103

Claims 1-18 and 20-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/61603 taken with Yoshioka *et al.* (U.S. Patent No. 4,347,316), Henco *et al.* (U.S. Patent No. 5,652,141) and Shah *et al.* (U.S. Patent No. 4,303,530). Office Action, page 3, lines 9-11. Applicants respectfully traverse the rejection.

To set forth a *prima facie* case of obviousness under 35 U.S.C. §103, the applied references must (among other requirements) teach or suggest all of the claim limitations. M.P.E.P., 8th ed., § 2143.03 (rev. 2, May 2004). The Examiner has set forth the above rejection by combining the primary reference (WO 99/61603) with Yoshioka *et al.*, Henco *et al.* and Shah *et al.* However, none of these references alone or in any proper combination teaches or suggests all of the claim limitations.

A. Primary Reference: WO 99/61603

The Examiner alleges that "WO 99/61603 discloses like the instantly claimed invention methods of separating and isolating proteins or peptide molecules and composition thereof from circular nucleic acid molecules (e.g., bacterial cells) via lysis and/or disruption under alkaline conditions at pH > 8 with a solid matrix consisting essentially of a silica matrix in presence of at least one chaotropic substance and one or more additional isolation procedures, such as filtration and/or chromatographic procedures (See e.g., pages 2, 5, 6, 8 and the examples and protocols) as directed to claims 1-3, 7, 8, 11-17 and 20." Office Action, page 3, lines 12-19. Applicants respectfully traverse this assertion.

All of Applicants' method claims as currently presented require that cells are contacted with a matrix which comprises one or more lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt or permeabilize the cells. Applicants' composition or kit claims also require that the matrix posess this property. In contrast, WO 99/61603 is limited to methods wherein *cells are lysed prior to contacting the silica. See* pages 8-9. Indeed, the Examiner has not indicated where the primary reference teaches or suggests contacting cells with one or more

lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt or permeabilize the cells.

Moreover, the allegation that WO 99/61603 discloses a method of separating and isolating proteins or peptide molecules is plainly incorrect. WO 99/61603 is entitled "Rapid and Simple Process for Isolation of Circular Nucleic Acids." This publication explicitly states that "[i]t is an object of this invention to provide a process for the isolation of circular nucleic acids, in particular plasmid DNA directly from sources containing such nucleic acids among other." Page 5, third full paragraph. Furthermore, the portions of this document referred to by the Examiner would not suggest to the skilled artisan that a method of separating proteins is disclosed. Rather, this reference pertains to separation and/or isolation of nucleic acids. *See* Abstract.

Therefore, WO 99/61603 is deficient in that it neither teaches nor suggests all of Applicants' claim limitations. As described in the sections which follow, this deficiency is not cured by any of the secondary references.

B. Secondary References

Although the Examiner combines WO 99/61603 with Yoshioka *et al.*, Henco *et al.* and Shah *et al.*, the secondary references also fail to teach or suggest Applicants' method claim limitation requiring that cells are contacted with a matrix which comprises one or more lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt or permeabilize the cells. The secondary references also fail to teach or suggest Applicants' composition or kit claims requiring that the matrix posess this property.

1. Yoshioka et al.

The Examiner relies upon Yoshioka *et al.* for a disclosure of "a process for isomerizing a glucose containing solution to co[n]vert a part of glucose to fructose by a method of isomerization in which the separation of fructose from the isomerized glucose solution may be carried out by conventional procedure." Office Action, page 4, last two lines to page 5, lines 1-2. Such a disclosure, however, has no relevance to the claimed method of separating proteins. Moreover, Applicants assert that there is no suggestion or motivation to combine Yoshioka *et al.*'s disclosure directed to processes of isomerizing glucose to fructose with the primary reference, WO 99/61603[1].

2. Shah et al.

The Examiner relies upon Shah *et al.* to " teach the use of a filter for removing microaggregates from the blood and blood components having a pore size and/or diameter of about 400 to [*sic*] microns (See e.g., cols 1-3) as directed to claims 4-6 and 28." Office Action, page 5, lines 8-10. Such a disclosure, however, has no relevance to the claimed method of separating proteins. The filters described by Shah *et al.* filter blood cells, *which are necessarily much larger than the proteins being separated according to Applicants' claims.*

Applicants also respectfully point out that Shah *et al.* fail to disclose lysing cells. In fact, such a process would defeat the express purpose of the disclosure of Shah *et al.*, which is directed to methods of separating intact blood cells for use in patients. *See, e.g.,* column 3, lines 38-44; and column 8, lines 23-62.

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1 The M.P.E.P. also indicates that a *prima facie* case of obviousness "requires that there be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." M.P.E.P., 8th ed., § 2143 (rev. May 2004).

Moreover, Applicants assert that there is no motivation to combine Shah *et al.*'s disclosure directed to blood filters with the primary reference, WO 99/61603.

3. Henco et al.

The Examiner relies upon Henco *et al.* to teach "the use of a device having matrix size from 1 to 50 μm in which the cell immobilized with matrix are lysed using detergent and eluted by adjusting to high ionic strength subsequent to various washing operations." Office Action, page 5, lines 12-13. Such a disclosure, however, has no relevance to the claimed method of separating proteins. Indeed, Henco *et al.* pertains to isolating nucleic acids from cells, not proteins. *See* title and abstract. Moreover, Applicants assert that there is no motivation to combine Henco *et al.*'s disclosure with the primary reference, WO 99/61603.

C. Summary of References Used in Rejection Under 35 U.S.C. § 103

Neither the primary or secondary references teach or suggest Applicants' method claim limitation requiring that cells are contacted with a matrix which comprises one or more lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt or permeabilize the cells. These references also fail to teach or suggest Applicants' composition or kit claims requiring that the matrix posess this property. Hence, because none of the applied references alone or in any proper combination teaches or suggests all of Applicants' claim limitations, a *prima facie* case of obviousness has not been set forth. Accordingly, Applicants request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §103.

II. Rejections Under 35 U.S.C. §112, 1st Paragraph

Claims 1-18 and 20-40 are rejected under 35 U.S.C. 112, first paragraph. Office Action, page 7. In particular, the Examiner alleges that the specification

> does not reasonably provide enablement for a method for separating and/or isolating of protein and peptide from high molecular weight molecules and structures, wherein said high molecular weight molecules or structures are selected from [the] group consisting of chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates of molecules and inclusion bodies, wherein one or more cells are selected from the group consisting of [] bacterial cells, yeast cells, fungal cells, animal cells, insect cells, mammalian cells, human cells, cells infected by a virus, transfected cells and plant cells, wherein one or more cells are bacterial cells of a genus selected from the group consisting of *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia and Caryophanon*, and compositions, apparatus and kits formulations thereof as recited in claims 1-18 and 20-40.

Office Action, page 7, lines 8-21. Applicants respectfully traverse the rejection.

Solely to expedite prosecution and not in acquiescence to the rejection, Applicants have amended the claims such that the recited at least one pore-containing matrix or composition comprises i) pores having a specified average size range and ii) a lysis/disruption/permeabilization composition or compound. As such, Applicants believe that the amendments render the rejection under 35 U.S.C. § 112, 1st paragraph moot. However, Applicants also provide the following comments traversing the rejection.

The M.P.E.P. provides guidance to examiners regarding enablement rejections. *See* M.P.E.P., 8th ed., § 2164 (Rev. 2, May 2004). In particular, the M.P.E.P. states that "[i]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." *Id.* at §2164.04 (*citing In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). The M.P.E.P. continues by reference to a Federal Circuit decision stating:

> A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as being in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

M.P.E.P., 8th ed., § 2164.04 (rev. May 2004, emphasis added) (*citing In re Marzocchi*, 439 F.2d 220, 223; 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

Applicants' specification clearly teaches the skilled artisan how to make or use the full scope of the invention as claimed. In particular, the specification states that proteins or peptides are isolated from high molecular weight molecules and structures (*see, e.g.*, pages 31-33) which includes chromosomal DNA, membrane fragments, liposomes, mitochondria, chloroplasts, ribosomes, aggregates and molecules and inclusion bodies. *See, e.g.*, paragraph 47, page 21.

The specification states that such isolation can be done from bacterial, yeast, fungal, animal, insect, mammalian, human, virally infected, transfected or plant cells. *See, e.g.*, paragraph 48, pages 21-22. The specification also states that bacterial cells can be selected from the genera *Escherichia, Bacillus, Staphylococcus, Agrobacter, Pseudomonas, Serratia* and *Caryophanon*. *See, e.g.*, paragraph 48, pages 21-22. Moreover, the ordinarily skilled artisan would expect that all of these cellular organisms have a similar architecture and will behave in a substantially similar manner with respect to Applicants' claims. All of these cellular organisms can be lysed for subsequent separation of proteins. The ordinarily skilled artisan upon reading Applicants' specification would not be required to undertake undue experimentation to determine how to lyse these types of cells and/or separate protein from high molecular weight molecules and structures.

Moreover, the M.P.E.P. states that whenever the Patent Office sets forth an enablement rejection under 35 U.S.C. §112, first paragraph, "it is incumbent upon the Patent Office . . . to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." M.P.E.P., 8th ed., § 2164.04 (rev. 2, May 2004, emphasis added) (*citing In re Marzocchi*, 439 F.2d 220, 223; 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

Here, the Examiner has concluded that the claims are not enabled without providing legally sufficient reasoning for such a conclusion. The Examiner has not identified what the ordinarily skilled artisan would appreciate as of the filing date of Applicants' application. The Examiner has not provided any documents or citations which might suggest that Applicants' specification fails to enable the claims. Indeed, the Examiner has only pointed to Applicants' specification in support of the non-enablement rejection. *Yet, nothing in Applicants' specification is inconsistent with the portions of Applicants' specification cited above.* These portions, among others, enable Applicants' claims.

The Examiner alleges that Applicants "acknowledge[] on page 1, last paragraph, by stating that lysis by physical methods produces membrane fragments and small DNA molecules caused by shearing of the chromosomal DNA, either of which can interfere with subsequent analysis of the desired proteins. Removal of these contaminants requires additional costly and time-consuming purification steps." Office Action, page 9, lines 16-20. The Examiner has taken this excerpt from the specification out of context.

This excerpt is found in Applicants' "Background Art" section (see Specification, page 1), and is provided solely as a contrast to Applicants' present invention. Applicants' characterizations of problems with the prior art are not applicable with respect to the enablement of Applicants' invention.

Thus, the Examiner has not set forth a *prima facie* case that the claims are not enabled by the specification. Moreover, the rejection is rendered moot by Applicants' amendments. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Aaron L. Schwartz
Attorney for Applicants
Registration No. 48,181

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

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